A Double-blind Study to Compare the Efficacy and Safety of Zonisamide and Carbamazepine as Monotherapy, in Newly Diagnosed Partial Epilepsy

This study has been completed.

Sponsor:
Eisai Inc.

Information provided by (Responsible Party):
Eisai Inc.

ClinicalTrials.gov Identifier:
NCT00477295

First received: May 21, 2007
Last updated: December 21, 2015
Last verified: November 2015
History of Changes

Results First Received: November 12, 2012

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Investigator); Primary Purpose: Treatment
Condition:	Epilepsy
Interventions:	Drug: Zonisamide Drug: Carbamazepine

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Zonisamide	The starting dose in this arm was zonisamide 100mg daily. The dose during the Titration Period (4 weeks) ranged from 100 to 200mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 300 to 500mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for

	26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.
Carbamazepine	The starting dose in this arm was carbamazepine 200mg daily. The dose during the Titration Period (4 weeks) ranged from 200 to 400mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 600 to 1200mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.

Participant Flow: Overall Study

	Zonisamide	Carbamazepine
STARTED	**282**	**301**
COMPLETED	**161**	**192**
NOT COMPLETED	**121**	**109**
Adverse Event	**31**	**35**
Withdrawal by Subject	**35**	**24**
Lack of Efficacy	**23**	**23**
Protocol Violation	**3**	**8**
Physician Decision	**4**	**5**
Lost to Follow-up	**21**	**11**
Not specified	**4**	**3**

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Zonisamide	The starting dose in this arm was zonisamide 100mg daily. The dose during the Titration Period (4 weeks) ranged from 100 to 200mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 300 to 500mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP(the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.
Carbamazepine	The starting dose in this arm was carbamazepine 200mg daily. The dose during the Titration Period (4 weeks) ranged from 200 to 400mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 600 to 1200mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.
Total	Total of all reporting groups

Baseline Measures

	Zonisamide	Carbamazepine	Total
Overall Participants Analyzed [Units: Participants]	**281**	**300**	**581**

Age [1] [Units: Years] Mean (Standard Deviation)	**37.1 (16.33)**	**35.6 (15.50)**	**36.4 (15.91)**
[1] Safety Population.			
Gender [1] [Units: Participants]			
Female	**107**	**128**	**235**
Male	**174**	**172**	**346**
[1] Safety Population: All randomized subjects who received at least one dose of study medication.			

Outcome Measures

Hide All Outcome Measures

1. Primary: Percentage of Participants Who Experienced Seizure Freedom for 26-weeks During the Maintenance Phase [Time Frame: Week 31 through Week 109]

Measure Type	Primary
Measure Title	Percentage of Participants Who Experienced Seizure Freedom for 26-weeks During the Maintenance Phase
Measure Description	A subject achieved a 26-week seizure-free period if they were free of all seizures, regardless of seizure type, for 26 weeks while receiving the same dose. The occurrence of seizures was documented in the seizure diary, which was maintained by the subject and reviewed at each following visit.
Time Frame	Week 31 through Week 109
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Per Protocol Population: All randomized subjects who received at least one dose of study medication and who had no major protocol violations.

Reporting Groups

	Description
Zonisamide	The starting dose in this arm was zonisamide 100mg daily. The dose during the Titration Period (4 weeks) ranged from 100 to 200mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 300 to 500mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP(the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.
Carbamazepine	The starting dose in this arm was carbamazepine 200mg daily. The dose during the Titration Period (4 weeks) ranged from 200 to 400mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 600 to 1200mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.

Measured Values

	Zonisamide	Carbamazepine
Participants Analyzed [Units: Participants]	**223**	**233**

Percentage of Participants Who Experienced Seizure Freedom for 26-weeks During the Maintenance Phase [Units: Percentage of Participants]	**79.4**	**83.7**

No statistical analysis provided for Percentage of Participants Who Experienced Seizure Freedom for 26-weeks During the Maintenance Phase

2. Secondary: Percentage of Participants Who Experienced Seizure Freedom for 12-months During the FDP and Maintenance Period [Time Frame: Week 5 through Week 109]

Measure Type	Secondary
Measure Title	Percentage of Participants Who Experienced Seizure Freedom for 12-months During the FDP and Maintenance Period
Measure Description	A subject achieved a 12-month seizure-free period if they were free of all seizures, regardless of seizure type, for 12 months while receiving the same dose. The occurrence of seizures was documented in the seizure diary, which was maintained by the subject and reviewed at each following visit.
Time Frame	Week 5 through Week 109
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Per Protocol Population. N=number of subjects with evaluable data.

Reporting Groups

	Description
Zonisamide	The starting dose in this arm was zonisamide 100mg daily. The dose during the Titration Period (4 weeks) ranged from 100 to 200mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 300 to 500mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP(the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.
Carbamazepine	The starting dose in this arm was carbamazepine 200mg daily. The dose during the Titration Period (4 weeks) ranged from 200 to 400mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 600 to 1200mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.

Measured Values

	Zonisamide	**Carbamazepine**
Participants Analyzed [Units: Participants]	**216**	**229**
Percentage of Participants Who Experienced Seizure Freedom for 12-months During the FDP and Maintenance Period [Units: Percentage of participants]	**67.6**	**74.7**

No statistical analysis provided for Percentage of Participants Who Experienced Seizure Freedom for 12-months During the FDP and Maintenance Period

3. Secondary: Analysis of Time to Drop Out Due to an Adverse Event (AE) [Time Frame: Week 1 through Week 109]

Measure Type	Secondary
Measure Title	Analysis of Time to Drop Out Due to an Adverse Event (AE)
Measure Description	An AE is defined as any untoward medical occurrence in a subject and does not necessarily have a causal relationship with the medicinal product. Adverse events were identified by: any unfavorable or unintended sign, symptom or disease temporarily associated with the use of a medicinal product; any new disease or exacerbation of an existing disease; any deterioration in nonprotocol-required measurements of laboratory values or other clinical test; and recurrence of an intermittent medical condition not present at Baseline.
Time Frame	Week 1 through Week 109
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Per Protocol Population

Reporting Groups

	Description
Zonisamide	The starting dose in this arm was zonisamide 100mg daily. The dose during the Titration Period (4 weeks) ranged from 100 to 200mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 300 to 500mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.
Carbamazepine	The starting dose in this arm was carbamazepine 200mg daily. The dose during the Titration Period (4 weeks) ranged from 200 to 400mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 600 to 1200mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.

Measured Values

	Zonisamide	**Carbamazepine**
Participants Analyzed [Units: Participants]	**223**	**233**
Analysis of Time to Drop Out Due to an Adverse Event (AE) [Units: Median Days] Median (Standard Error)	**NA** [1]	**NA** [1]

[1] Please note that this is reported as 'Not Calculable' due to insufficient events.

No statistical analysis provided for Analysis of Time to Drop Out Due to an Adverse Event (AE)

4. Secondary: Analysis of Time to Drop Out Due to Lack of Efficacy [Time Frame: Week 1 through Week 109]

Measure Type	Secondary
Measure Title	Analysis of Time to Drop Out Due to Lack of Efficacy
Measure Description	Lack of efficacy was evaluated by the subject and on the basis of whether zonisamide and carbamazepine gave the subject at least a 26-week seizure free rate. The subject could withdraw at any time due to lack of efficacy.
Time Frame	Week 1 through Week 109
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Per Protocol Population

Reporting Groups

	Description
Zonisamide	The starting dose in this arm was zonisamide 100mg daily. The dose during the Titration Period (4 weeks) ranged from 100 to 200mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 300 to 500mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.
Carbamazepine	The starting dose in this arm was carbamazepine 200mg daily. The dose during the Titration Period (4 weeks) ranged from 200 to 400mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 600 to 1200mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.

Measured Values

	Zonisamide	Carbamazepine
Participants Analyzed [Units: Participants]	**223**	**233**
Analysis of Time to Drop Out Due to Lack of Efficacy [Units: Median Days] Median (Standard Error)	**722** [1]	**NA** [1]

[1] Please note that this is reported as 'Not Calculable' due to insufficient events.

No statistical analysis provided for Analysis of Time to Drop Out Due to Lack of Efficacy

5. Secondary: Time to 6-months Seizure Freedom [Time Frame: Week 5 through Week 83]

Measure Type	Secondary
Measure Title	Time to 6-months Seizure Freedom
Measure Description	A subject achieved a 6-months seizure-free period if they were free of all seizures, regardless of seizure type, for 6-months while receiving the same dose. The occurrence of seizures was documented in the seizure diary, which was maintained by the subject and reviewed at each following visit.
Time Frame	Week 5 through Week 83
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent-to-Treat (ITT) Population - randomized subjects who received at least one dose of study medication.

Reporting Groups

	Description

Zonisamide	The starting dose in this arm was zonisamide 100mg daily. The dose during the Titration Period (4 weeks) ranged from 100 to 200mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 300 to 500mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.
Carbamazepine	The starting dose in this arm was carbamazepine 200mg daily. The dose during the Titration Period (4 weeks) ranged from 200 to 400mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 600 to 1200mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.

Measured Values

	Zonisamide	**Carbamazepine**
Participants Analyzed [Units: Participants]	**281**	**300**
Time to 6-months Seizure Freedom [Units: Days] Mean (Standard Deviation)	**222.7 (49.78)**	**220.4 (46.31)**

No statistical analysis provided for Time to 6-months Seizure Freedom

6. Secondary: Time to 12-months Seizure Freedom [Time Frame: Week 5 through Week 83]

Measure Type	Secondary
Measure Title	Time to 12-months Seizure Freedom
Measure Description	A subject achieved a 12-month seizure-free period if they were free of all seizures, regardless of seizure type, for 12-months while receiving the same dose. The occurrence of seizures was documented in the seizure diary, which was maintained by the subject and reviewed at each following visit.
Time Frame	Week 5 through Week 83
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
ITT Population

Reporting Groups

	Description
Zonisamide	The starting dose in this arm was zonisamide 100mg daily. The dose during the Titration Period (4 weeks) ranged from 100 to 200mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 300 to 500mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.
Carbamazepine	The starting dose in this arm was carbamazepine 200mg daily. The dose during the Titration Period (4 weeks) ranged from 200 to 400mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 600 to 1200mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the

	Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.

Measured Values

	Zonisamide	Carbamazepine
Participants Analyzed [Units: Participants]	**281**	**300**
Time to 12-months Seizure Freedom [Units: Days] Mean (Standard Deviation)	**399.3 (55.03)**	**395.6 (42.19)**

No statistical analysis provided for Time to 12-months Seizure Freedom

7. Secondary: Change From Baseline in Total ABNAS Score at Maintenance Period Visit 1 [Time Frame: Baseline and Maintenance Period Visit 1 (Week 31 to Week 83)]

Measure Type	Secondary
Measure Title	Change From Baseline in Total ABNAS Score at Maintenance Period Visit 1
Measure Description	The Aldenkamp-Baker Neuropsychological Assessment Scale(ABNAS) is a subject based questionnaire to measure subjective perceived drug-related cognitive impairments. The ABNAS measured seven critical domains of cognition(tiredness/fatigue,hyperexcitability, slowing(mental and motor),memory impairment,attention disorders,impairment of motor coordination, and language disorders). The total score ranged from 0 to 72, with a higher score reflecting a high level of problems.
Time Frame	Baseline and Maintenance Period Visit 1 (Week 31 to Week 83)
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent-to-Treat Population: All randomized subjects who received at least one dose of study medication. This was measured using Observed Case (OC).

Reporting Groups

	Description
Zonisamide	The starting dose in this arm was zonisamide 100mg daily. The dose during the Titration Period (4 weeks) ranged from 100 to 200mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 300 to 500mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.
Carbamazepine	The starting dose in this arm was carbamazepine 200mg daily. The dose during the Titration Period (4 weeks) ranged from 200 to 400mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 600 to 1200mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.

Measured Values

	Zonisamide	Carbamazepine
Participants Analyzed		

[Units: Participants]	**281**	**300**
Change From Baseline in Total ABNAS Score at Maintenance Period Visit 1 [Units: Scores on a Scale] Mean (Standard Deviation)	**1.6 (15.43)**	**-0.1 (12.71)**

No statistical analysis provided for Change From Baseline in Total ABNAS Score at Maintenance Period Visit 1

8. Secondary: Change From Baseline in Bond and Lader VAS Mood Sub-Scores at Maintenance Period Visit 1 [Time Frame: Baseline and Maintenance Period Visit 1 (Week 31 to Week 83)]

Measure Type	Secondary
Measure Title	Change From Baseline in Bond and Lader VAS Mood Sub-Scores at Maintenance Period Visit 1
Measure Description	The Bond-Lader Visual Analogue Scale (VAS) is made up of 16 pairs of alternative descriptors of mood and attention at either end of a 10 cm line. Subjects were asked to rate their feelings at the time of assessment by indicating the point on the line which best represent their mood. Each item was scored by measuring the position relative to the left hand end of the line and levels of anxiety, sedation, and dysphoria were then calculated from the combined scores of selected items. The scores ranged from 0 to 100, with a high score reflecting a high level of anxiety, sedation or dysphoria.
Time Frame	Baseline and Maintenance Period Visit 1 (Week 31 to Week 83)
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent-to-Treat Population. This was measured using Observed Case (OC).

Reporting Groups

	Description
Zonisamide	The starting dose in this arm was zonisamide 100mg daily. The dose during the Titration Period (4 weeks) ranged from 100 to 200mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 300 to 500mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.
Carbamazepine	The starting dose in this arm was carbamazepine 200mg daily. The dose during the Titration Period (4 weeks) ranged from 200 to 400mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 600 to 1200mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.

Measured Values

	Zonisamide	**Carbamazepine**
Participants Analyzed [Units: Participants]	**281**	**300**
Change From Baseline in Bond and Lader VAS Mood Sub-Scores at Maintenance Period Visit 1 [Units: Scores on a Scale] Mean (Standard Deviation)		
Anxiety	**-2.036 (23.6120)**	**-1.993 (26.1087)**

Sedation	**-0.475 (21.7476)**	**-1.362 (18.0103)**
Dysphoria	**-1.930 (21.7585)**	**-3.833 (19.7824)**

No statistical analysis provided for Change From Baseline in Bond and Lader VAS Mood Sub-Scores at Maintenance Period Visit 1

9. Secondary: Change From Baseline in QOLIE-31-P Overall Score at Maintenance Period Visit 1 [Time Frame: Baseline and Maintenance Period Visit 1 (Week 31 to Week 83)]

Measure Type	Secondary
Measure Title	Change From Baseline in QOLIE-31-P Overall Score at Maintenance Period Visit 1
Measure Description	The Quality of Life in Epilepsy - Problems(QOLIE-31-P) was completed by the patient and contained 30 items covering seven subscales(seizure worry, overall Quality of Life (QOL),emotional well-being,energy-fatigue, cognition,medication effects and social function) and one item covering health status. It also included seven items addressing overall distress related to each subscale, an item addressing the relative importance of each subscale topic, and an item addressing perception of overall change in QOL at the end of the study. A high score reflects a good QOL. The following scale range is a sample of 1 of the 7 of the subscales: 10 (Best possible quality of life) - 0 (Worst possible quality of life); Rand Corporation QOLIE-31 Scoring Manual was used. The QOLIE-31 overall score is calculated by summing the product of each scale score times its weight and summing overall all scales.
Time Frame	Baseline and Maintenance Period Visit 1 (Week 31 to Week 83)
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent-to-Treat Population. This was measured using Observed Case (OC).

Reporting Groups

	Description
Zonisamide	The starting dose in this arm was zonisamide 100mg daily. The dose during the Titration Period (4 weeks) ranged from 100 to 200mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 300 to 500mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.
Carbamazepine	The starting dose in this arm was carbamazepine 200mg daily. The dose during the Titration Period (4 weeks) ranged from 200 to 400mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 600 to 1200mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.

Measured Values

	Zonisamide	**Carbamazepine**
Participants Analyzed [Units: Participants]	**281**	**300**
Change From Baseline in QOLIE-31-P Overall Score at Maintenance Period Visit 1 [Units: Scores on a Scale] Mean (Standard Deviation)	**4.474 (15.2838)**	**6.090 (13.2861)**

No statistical analysis provided for Change From Baseline in QOLIE-31-P Overall Score at Maintenance Period Visit 1

10. Secondary: Change From Baseline in SF-36 Aggregate Mental and Physical Component Score at Maintenance Period Visit 1 [Time Frame: Baseline and Maintenance Period Visit 1 (Week 31 to Week 83)]

Measure Type	Secondary
Measure Title	Change From Baseline in SF-36 Aggregate Mental and Physical Component Score at Maintenance Period Visit 1
Measure Description	The Short Form 36 Health and Well-Being Questionnaire (SF-36) is a 36-item generic health related QOL instrument covering the following domains: physical functioning, role-physical,bodily pain, general health, social functioning,role-emotional, mental health, and vitality. It yields a profile of eight scores, one for each domain, and physical and mental health summary measures. Each domain is described by a score ranging from 0 to 100, for a range of total possible scoes of 0-400 for physical and 0-400 for mental. An increase represents an improvement, whereas a decrease reflects a worsening.
Time Frame	Baseline and Maintenance Period Visit 1 (Week 31 to Week 83)
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent-to-Treat Population. This was measured using Observed Case (OC).

Reporting Groups

	Description
Zonisamide	The starting dose in this arm was zonisamide 100mg daily. The dose during the Titration Period (4 weeks) ranged from 100 to 200mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 300 to 500mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.
Carbamazepine	The starting dose in this arm was carbamazepine 200mg daily. The dose during the Titration Period (4 weeks) ranged from 200 to 400mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 600 to 1200mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.

Measured Values

	Zonisamide	**Carbamazepine**
Participants Analyzed [Units: Participants]	**281**	**300**
Change From Baseline in SF-36 Aggregate Mental and Physical Component Score at Maintenance Period Visit 1 [Units: Scores on a Scale] Mean (Standard Deviation)		
Aggregate Mental Component Score	**1.027 (10.9124)**	**2.495 (10.5310)**
Aggregate Physical Component Score	**1.895 (7.6287)**	**2.041 (6.2613)**

No statistical analysis provided for Change From Baseline in SF-36 Aggregate Mental and Physical Component Score at Maintenance Period Visit 1

11. Secondary: Percentage of Participants With EQ-5D Scores at Maintenance Period Visit 1 [Time Frame: Week 31 through Week 83]

Measure Type	Secondary
Measure Title	Percentage of Participants With EQ-5D Scores at Maintenance Period Visit 1
Measure Description	The European Quality of Life Group 5-Dimension Self-Report Questionnaire (EQ-5D) is a preference based generic health related quality of life (HRQoL) instrument which classifies health states across five domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each domain has three levels, they are (1) no problems, (2) some problems, (3) extreme problems. The percentages shown are calculated from the number of subjects at that visit with non-missing data for that score.
Time Frame	Week 31 through Week 83
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent-to-Treat Population. This was measured using Observed Case (OC). The percentages shown are calculated from the number of subjects at that visit with non-missing data for that score (n=174,196).

Reporting Groups

	Description
Zonisamide	The starting dose in this arm was zonisamide 100mg daily. The dose during the Titration Period (4 weeks) ranged from 100 to 200mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 300 to 500mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.
Carbamazepine	The starting dose in this arm was carbamazepine 200mg daily. The dose during the Titration Period (4 weeks) ranged from 200 to 400mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 600 to 1200mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.

Measured Values

	Zonisamide	**Carbamazepine**
Participants Analyzed [Units: Participants]	**174**	**196**
Percentage of Participants With EQ-5D Scores at Maintenance Period Visit 1 [Units: Percentage of Participants]		
Mobility: No problems	**90.8**	**86.7**
Mobility: Some problems	**8.7**	**12.9**
Mobility: Confined to Bed	**0.5**	**0.5**
Self-Care:No problems	**96.7**	**97.6**
Self-Care: Some problems	**2.7**	**2.4**
Self-Care: Unable to wash or dress	**0.5**	**0.0**
Usual Activities: No problems	**89.1**	**84.8**
Usual Activities: Some problems	**9.8**	**15.2**
Usual Activities: Unable to perform	**1.1**	**0.0**
Pain/Discomfort: None	**75.5**	**73.2**
Pain/Discomfort: Moderate	**22.3**	**25.4**

Pain/Discomfort: Extreme	2.2	1.4
Anxiety/Depression: None	64.3	62.9
Anxiety/Depression: Moderate	31.3	34.8
Anxiety/Depression: Extreme	4.4	2.4

No statistical analysis provided for Percentage of Participants With EQ-5D Scores at Maintenance Period Visit 1

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	A Treatment-Emergent Adverse Event (TEAE) is an Adverse Event (AE) with a start date on or after Day 1 and within 15 days of last dose, including AEs with missing start dates, for up to 116 weeks.
Additional Description	For each AE category, a subject with two or more adverse events in that category is only counted once.

Reporting Groups

	Description
Zonisamide	The starting dose in this arm was zonisamide 100mg daily. The dose during the Titration Period (4 weeks) ranged from 100 to 200mg daily. During the Flexible Dosing Period (FDP), the subjects were given doses ranging from 300 to 500mg daily or if they could not tolerate that dose, were allowed one down-titration or were withdrawn. If the subjects remained seizure-free for 26 weeks by the end of FDP (the subject was allowed 3 chances to achieve this), they entered the Maintenance Period (26 weeks), where they remained on the same dose they were taking at the end of the FDP.
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Serious Adverse Events

	Zonisamide	Carbamazepine
Total, serious adverse events		
# participants affected / at risk	**15/281 (5.34%)**	**17/300 (5.67%)**
Cardiac disorders		
Bradycardia † 1		
# participants affected / at risk	**0/281 (0.00%)**	**1/300 (0.33%)**
Myocardial infarction † 1		
# participants affected / at risk	**1/281 (0.36%)**	**0/300 (0.00%)**
Ear and labyrinth disorders		
Vertigo † 1		
# participants affected / at risk	**1/281 (0.36%)**	**0/300 (0.00%)**
Gastrointestinal disorders		
Gastric ulcer † 1		
# participants affected / at risk	**0/281 (0.00%)**	**1/300 (0.33%)**
General disorders		
Death † 1		
# participants affected / at risk	**1/281 (0.36%)**	**0/300 (0.00%)**

Pyrexia † 1		
# participants affected / at risk	1/281 (0.36%)	0/300 (0.00%)
Hepatobiliary disorders		
Cholelithiasis † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)
Infections and infestations		
Appendicitis † 1		
# participants affected / at risk	1/281 (0.36%)	0/300 (0.00%)
Chronic sinusitis † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)
Sinusitis bacterial † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)
Typhoid fever † 1		
# participants affected / at risk	1/281 (0.36%)	0/300 (0.00%)
Injury, poisoning and procedural complications		
Facial bones fracture † 1		
# participants affected / at risk	0/281 (0.00%)	2/300 (0.67%)
Femur fracture † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)
Head injury † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)
Humerus fracture † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)
Joint dislocation † 1		
# participants affected / at risk	1/281 (0.36%)	0/300 (0.00%)
Muscle strain † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)
Radius fracture † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)
Skull fracture † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)
Investigations		
Hepatic enzyme increased † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)
Metabolism and nutrition disorders		
Hypokalemia † 1		
# participants affected / at risk	1/281 (0.36%)	0/300 (0.00%)
Musculoskeletal and connective tissue disorders		
Bone pain † 1		
# participants affected / at risk	1/281 (0.36%)	0/300 (0.00%)
Musculoskeletal pain † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Brain neoplasm † 1		
# participants affected / at risk	1/281 (0.36%)	0/300 (0.00%)

Prostate cancer † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)
Nervous system disorders		
Partial seizures with secondary generalization † 1		
# participants affected / at risk	0/281 (0.00%)	4/300 (1.33%)
Complex partial seizures † 1		
# participants affected / at risk	1/281 (0.36%)	0/300 (0.00%)
Convulsion † 1		
# participants affected / at risk	1/281 (0.36%)	0/300 (0.00%)
Epilepsy † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)
Ischemic stroke † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)
Partial seizures † 1		
# participants affected / at risk	1/281 (0.36%)	0/300 (0.00%)
Subarachnoid hemorrahage † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)
Psychiatric disorders		
Acute psychosis † 1		
# participants affected / at risk	1/281 (0.36%)	0/300 (0.00%)
Suicidal ideation † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)
Suicide attempt † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)
Respiratory, thoracic and mediastinal disorders		
Nasal septum deviation † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)
Respiratory disorder † 1		
# participants affected / at risk	1/281 (0.36%)	0/300 (0.00%)
Rhinitis hypertrophic † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)
Skin and subcutaneous tissue disorders		
Rash † 1		
# participants affected / at risk	0/281 (0.00%)	2/300 (0.67%)
Purpura † 1		
# participants affected / at risk	1/281 (0.36%)	0/300 (0.00%)
Vascular disorders		
Hypotension † 1		
# participants affected / at risk	0/281 (0.00%)	1/300 (0.33%)

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA v. 10.1

Other Adverse Events

Hide Other Adverse Events

Time Frame	A Treatment-Emergent Adverse Event (TEAE) is an Adverse Event (AE) with a start date on or after Day 1 and within 15 days of last dose, including AEs with missing start dates, for up to 116 weeks.
Additional Description	For each AE category, a subject with two or more adverse events in that category is only counted once.

Frequency Threshold

Threshold above which other adverse events are reported	5

Reporting Groups

	Description
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Other Adverse Events

	Zonisamide	Carbamazepine
Total, other (not including serious) adverse events		
# participants affected / at risk	**72/281 (25.62%)**	**69/300 (23.00%)**
Investigations		
weight decreased † 1		
# participants affected / at risk	**19/281 (6.76%)**	**0/300 (0.00%)**
Metabolism and nutrition disorders		
decreased appetite † 1		
# participants affected / at risk	**22/281 (7.83%)**	**5/300 (1.67%)**
Nervous system disorders		
headache † 1		
# participants affected / at risk	**29/281 (10.32%)**	**37/300 (12.33%)**
somnolence † 1		
# participants affected / at risk	**17/281 (6.05%)**	**23/300 (7.67%)**
dizziness † 1		
# participants affected / at risk	**11/281 (3.91%)**	**23/300 (7.67%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA v. 10.1

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data

No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.

There is **NOT** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

Results Point of Contact:

Name/Title: Eisai Inc.
Organization: Eisai Call Center
phone: 888-422-4743

Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Baulac M, Brodie MJ, Patten A, Segieth J, Giorgi L. Efficacy and tolerability of zonisamide versus controlled-release carbamazepine for newly diagnosed partial epilepsy: a phase 3, randomised, double-blind, non-inferiority trial. Lancet Neurol. 2012 Jul;11(7):579-88. doi: 10.1016/S1474-4422(12)70105-9.

Responsible Party:	Eisai Inc.
ClinicalTrials.gov Identifier:	NCT00477295 History of Changes
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	2006-000156-40 (EudraCT Number)
Study First Received:	May 21, 2007
Results First Received:	November 12, 2012
Last Updated:	December 21, 2015
Health Authority:	European Union: European Medicines Agency

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